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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/211,315	12/14/98	BOYLE W	A-451-G

HM12/0224

US PATENT OPERATIONS/RBW
DEPT 430 M/S 27-4-A
AMGEN INC
ONE AMGEN CENTER DRIVE
THOUSAND OAKS CA 91320-1799

EXAMINER	
TURNER,S	
ART UNIT	**PAPER NUMBER**
1644	11

DATE MAILED: 02/24/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/211,315	Applicant(s) Boyle
	Examiner Sharon L. Turner, Ph.D.	Group Art Unit 1644

☒ Responsive to communication(s) filed on *12-10-99*

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *37-49* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *37-49* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

Response to Amendment

1. The Examiner and/or Art Unit of U.S. Patent application SN 09/211,315 has changed. In order to expedite the correlation of papers with the application please direct all future correspondence to Examiner Turner, Technology Center 1600, Art Unit 1644.

2. The amendment filed 12-10-99 has been entered into the record and has been fully considered.

3. As a result of applicants amendment, all rejections not reiterated herein have been withdrawn by the examiner.

Rejections Maintained

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 37-49 stand rejected under 35 U.S.C. 112, first paragraph, as set forth in Paper No. 8, mailed 6-8-99 as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant argues that the specification discloses the biological function of osteoprotegrin binding protein (OPGbp) and the effects of blocking OPGbp, that modulators of OPGbp activity

which are either agonists or antagonists are readily identified by assays such as those described in Examples 8 and 9, that the application teaches OPGbp modulators and antibodies, that the specification teaches one skilled in the art how to obtain a modulator of OPGbp and to evaluate the properties of said modulator on in vitro and in vivo OPGbp activity, and that in particular the specification teaches the production of antibodies which bind OPGbp and identify either antibody agonists and antagonists of OPGbp activity.

These arguments have been considered but are not persuasive for the reasons made of record and as further discussed herein. Applicants have disclosed that OPGbp administration causes bone resorption in vivo. Osteoprotegrin (OPG) is recognized to promote bone formation. Applicants have shown that OPG administration decreases the amount of bone resorption seen after OPGbp administration. However, the claims recite a method of inhibiting bone resorption in a mammal comprising administering a modulator of an osteoprotegerin binding protein, wherein the modulator is an antibody or fragment thereof which binds an osteoprotegerin binding protein. The experiment, disclosed in Example 9 (*administration of OPG* to reverse the bone resorption effects seen in mice following administration of OPGbp), differs from the method claimed, *administration of an antibody which binds OPGbp*. There are no examples given in the specification whereby antibody to OPGbp is shown to modulate bone resorption. Takahishi et al, Biochem. and Biophys. Res. Comm., 256:449-55, 1999 teach that osteoclastic bone resorption consists of two major processes: one is the recruitment of new osteoclasts and the other is the activation of mature osteoclasts, see p. 449, col. 1, lines 14-15, in particular. The specification

does not teach that administration of an OPGbp antibody affects these processes. Ligand-receptor interactions are complex and the skilled artisan can not predict how the binding of an antibody to any ligand will enhance or inhibit the affinity or binding of that ligand to its receptor. In addition, one can not predict the altered signal properties of the receptor upon binding a ligand bound by an antibody. The method instantly claimed is not enabled because contrary to applicants assertion the specification has not taught how to identify, predict or screen for those antibodies which not only bind OPGbp, but modulate OPGbp activity such that bone resorption is inhibited. Applicants arguments appear to assume that all antibodies to OPGbp will bind to block the bone resorption activity of OPGbp, thus inhibiting bone resorption. However applicants fail to test this hypothesis and contrary to applicants assertion do not teach that an OPGbp antibody either in vitro or in vivo can exhibit anti-bone resorption activities. The administration of OPG (a decoy receptor, see Takahashi et al, Figure 1, 2) to animals does not aid the skilled artisan in determining those antibodies that will inhibit bone resorption from those that enhance bone resorption as a result of binding OPGbp. Applicants have not disclosed any antibodies which bind and act as either agonists or antagonists of bone resorptive activity. There are no antibodies utilized in Example 8 or Example 9. The only antibodies discussed in applicants specification are those hypothetically generated in Example 11, see specification, p. 47-51. Thus, in view of the quantity of experimentation necessary to identify those antibodies which bind and inhibit bone resorptive activity, the lack of any working examples using such antibodies either in vitro or in vivo, the impredictability of the art with respect to ligand-receptor

and decoy receptor interactions, the lack of sufficient guidance in the specification and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

Status of Claims

6. No claims are allowed.

Conclusion

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

8. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharon L. Turner, Ph.D. whose telephone number is (703) 308-0056. The examiner can normally be reached on Monday-Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973.

Sharon L. Turner, Ph.D.
February 23, 2000

PATRICIA A. DUFFY
PRIMARY EXAMINER